UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

LAURA ALLEN, INDIVIDUALLY AND AS ADMINISTRATRIX OF THE ESTATE OF DAN ALLEN, AND AS NEXT FRIEND TAYLOR ALLEN AND DANIELLE ALLEN; AND MARK ALLEN Plaintiffs, v. MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES, INC; SOUTHWEST RECREATIONAL INDUSTRIES, INC ., d/b/a MARTIN SURFACING; Defendants.	CIVIL ACTION NO. 05-40048-FDS

PLAINTIFFS' OMNIBUS OPPOSITION TO DEFENDANT'S MOTIONS TO EXCLUDE EXPERTS' TESTIMONY AT TRIAL

I. INTRODUCTION

Counsel for the defendant has filed three separate *Daubert*/summary judgment motions to strike each of plaintiff's causation experts: Marcia Ratner, Christine Oliver and William Ewing[1]. Each motion, however, makes the same essential assertions: (a) the expert is not qualified; (b) the expert's "general causation" opinion -- that the solvents to which Coach Allen was exposed are capable of hastening the early onset of his ALS -- is speculative; and (c) the expert's "specific causation" opinion -- that these solvents were indeed at least a substantial contributing factor to hastening the early onset of the ALS -- is speculative.

[1] As a practical matter, plaintiffs treat these motions solely as *Daubert* motions; that is, summary judgment would not be ripe unless the *Daubert* motions were allowed in full.

Because each defense motion makes the same general assertions as to each expert, the plaintiffs present here one "omnibus" opposition, for the convenience of the court. We have set forth below our arguments that apply generally in opposition to all three of the defense motions, but we have also presented expert-specific oppositions whenever necessary, as delineated.

The defendant's attack on plaintiffs' experts can be distilled down to the following six primary arguments:

1. Plaintiffs' experts must specifically be experts in the relationship between toluene (or other solvents) and ALS;

2. If science has not yet identified the known causes of ALS, one cannot prove that a solvent hastens the early onset of ALS;

3. Epidemiology is the science which controls the questions in this case, and there is no epidemiology which demonstrates that specific solvents like toluene cause or hasten the early onset of ALS;

4. Plaintiffs must prove in this case that toluene (or any other solvent at issue) was "the actual and proximate cause" which hastened the early onset of Coach Allen's ALS;

5. Plaintiffs must, but cannot, show the specific level of Coach Allen's exposure to toluene (or any other solvent at issue);

6. Ratner and Oliver's theory of causation is novel and created solely for purposes of this lawsuit.

All these "scientific" assertions, in turn, have two things in common:

1. The scientific assertions are all the *ipse dixit* of defense counsel. In other words, defense counsel fails to support <u>any</u> of the above scientific assertions with scientific citations, whether to his own expert (his report, his deposition or by affidavit), textbooks, journals, or otherwise; and more importantly,

2. They are all wrong, for the reasons set forth below.

Moreover, the legal assertions are based on case law from other jurisdictions which are not controlling and/or not accurately represented, as well as case law from Massachusetts which, again, is not accurately represented and ignores other case law on point.

Plaintiffs previously filed, affirmatively, **PLAINTIFFS' MOTION TO FULLY INCLUDE THEIR CAUSATION EXPERTS' TESTIMONY AT TRIAL** (hereafter "**Plaintiffs' Affirmative Motion**"). Attached to that motion are all the expert reports, CVs and other material which support plaintiffs' position in opposition here, and are incorporated by reference. Only new exhibits to this pleading are attached here.

II. ARGUMENT No. 1: QUALIFICATIONS

The 1st Circuit has made it clear that "there is no mechanical checklist for measuring whether an expert is qualified to offer opinion evidence in a particular field. . .The test is whether, under the totality of the circumstances, the witness can be said to be qualified as an expert in a particular field through any one or more of the five bases enumerated in *Rule 702* – knowledge, skill experience, training or education." *Santos v. Posadas de Puerto Rico Assoc., Inc.*, 452 F.3d 59 (1st Cir. 2006).

The defendant cites to *Whiting v. Boston Edison Co.*, 891 F. Supp. 12 (D. Mass. 1995) for the proposition that, if plaintiffs' experts are not experts specifically in ALS and Toluene, they are not qualified. In *Whiting*, a nuclear power plant station worker died from a form of leukemia called ALL; his estate sued the power plant asserting that radiation caused the ALL. Plaintiff offered two experts, an epidemiologist/occupational health physician and an internist. Central to that case was a determination whether the radiation exposure exceeded the permissible levels set by the federal government, as the levels of exposure actually recorded by the power plant were within those permissible

limits; plaintiff was asserting those recordings were inaccurate. The method for assessing levels of radiation exposure is called "dosimetry" and can be employed only by a very specialized field called "health physics"; neither of plaintiff's experts were health physicists and therefore, neither was qualified in to offer opinions as to whether the exposure exceeded, or was any different than the recorded levels. Similarly, the internist had no expertise in hematology or oncology, the general areas of medicine which concern leukemia.

In *Whiting*, Judge Stearns, without citation, did state that, "a witness must be qualified in the specific subject for which his testimony is offered", but clearly, he was referring to the lack of dosimetry expertise; he implicitly acknowledged that general expertise in hematology/oncology would be sufficient to address issues about the sub-topic leukemia. This statement was not applied in *Whiting* with the rigidity the defense hopes to apply here.

Indeed, the First Circuit has made it quite clear that "Rule 702 is not so wooden as to demand an intimate level of familiarity with every component of a transaction or device as a prerequisite to offering expert testimony" and so long as the expert is qualified by their knowledge, skill experience, training and education, "he need not have had first-hand dealings with the precise type of event that is at issue." *Microfinancial, Inc. v. Premier Holidays Intern, Inc.*, 385 F. 3d 72 (1st Cir. 2004); *Mitchell v. U.S.*, 141 F. 3d 8 (1st Cir. 1998)(in medical malpractice action, internist could testify about defendant physician's treatment of patient, even though not a gastroenterologist).

Plaintiffs' experts, by their knowledge, skill experience, training and education, are in fact some of the most qualified persons in their fields, which are directly relevant to the issues in this matter:

A. Marcia Ratner

Dr. Ratner's professional education, experience and training have created a unique combination of clinical, academic and laboratory-based expertise in the very subject matter at issue in this legal case: assessing the role of an exposure to neurotoxic chemicals to the onset of a neurodegenerative disease. As Dr. Ratner will explain in-person to the Court, there are few scientists in the country with this clinical/academic/bench-science background.

In 2004, Dr. Ratner earned her Ph.D. from Boston University School of Medicine's Behavioral Neurosciences Program. She trained and worked directly with the late Robert Feldman, M.D., generally considered one of, if not the world's foremost experts in neurotoxicology. From 1998-2004, she was the Senior Toxicologist and Project Manager working in conjunction with Dr. Feldman under the Department of Neurology's Environmental and Occupational Neurology Program. Their work resulted in several articles, textbook chapters and other professional writings, most of which are peer-reviewed, on the subject of neurotoxicology and neurodegenerative disorders. Dr. Ratner is the co-author of those writings. Today, she remains the Senior Toxicologist for the Environmental and Occupational Neurology Program at the Boston University School of Medicine.

Between 2004 and 2007, Dr. Ratner conducted and completed a post-doctoral fellowship supported by an NIH training grant in Aging, in the Laboratory of Molecular

Neurobiology within the Department of Pharmacology and Experimental Therapeutics at the Boston University School of Medicine. She focuses her work in the lab in assessing the *in vivo* effects of novel chemicals, which may be developed into new drugs to address neurological and psychiatric disorders, including neurodegenerative diseases. In that capacity, she has become an expert in the toxicological and pharmacological methods used by academic and industrial researchers to assess the ability of chemicals to alter the course of neurological disease. **Currently, Dr. Ratner and her colleagues are in fact researching a new drug with the potential to treat ALS, the precise disease at issue here.**

Since 2004, Dr. Ratner has been a research associate in the Department of Pharmacology and Experimental Therapeutics. In that regard, she is well studied and experienced in: (a) the scientific method for research; (b) biostatistics and epidemiology; the ability to understand and apply the results of scientific studies to consideration of causal assessment; and (c) assessing the quality of scientific studies.

Since 1998, she has been a research associate in the Department of Neurology at the Boston University School of Medicine. In that role, she has worked as a clinical research scientist evaluating patients with neurological conditions, including neurodegenerative disease such as ALS. She has worked closely with Dr. Joseph Jabre, the former chair of neurology at the VA Hospital and a faculty member at the School of Medicine at Boston University. As a research associate, Dr. Ratner is well-versed and experienced in the diagnosis and treatment of patients with neurodegenerative disorders. She is fully competent in performing clinical evaluations of such patients, contrary to the bald assertion of defense counsel.

In recognition of her cross-over background in clinical neurology, pharmacology and expertise in neurotoxicology, Dr. Ratner has been invited to lecture classes at the Boston University School of Medicine's Departments of Neurology, Biochemistry, Environmental Health, Behavioral Neuroscience Program; in addition, she has been an invited lecturer at the Harvard School of Public Health and the Massachusetts Neuropsychological Society. Dr. Ratner has lectured to these classes in the following topics: Neurological Disorders and Neurotoxicology, Forensic Neuropsychology, Introductory Toxicology, Forensic Toxicology, and Neurotoxicity.

The defense motion describes Dr. Ratner's research focus as limited to the association between neurotoxins and Parkinson's disease. This is not true. Dr. Ratner is widely recognized as an expert in her field of study: the association between neurotoxins and neurodegenerative disorders. By way of example, in a peer-reviewed paper published in the *Archives of Neurology* in June 2005 (before this lawsuit commenced) examining whether environmental factors played a role in the initiation of a different neurodegenerative disorder (Huntington disease), Dr. Ratner was expressly recognized by the authors for "her help in understanding the toxicity analysis". See **Tab 1**.

The defense motion also asserts that Dr. Ratner cannot testify to a "reasonable degree of medical certainty" on any given opinion because she is not a licensed physician. Defense offers no case law in support of this assertion. While it is true that she is not a licensed medical doctor, Dr. Ratner was educated in a medical school and has been adequately trained in the diagnosis of disease and its etiology: (a) she took the same Neurosciences course as all the MD students at the Boston University School of Medicine; (b) the course work she took included training in the performance and

interpretation of the results of a neurological exam and neurobehavioral testing data; (c) she spent seven years training alongside neurology residents in the Department of Neurology; (d) during her training she attended weekly grand rounds in neurology, attended clinic with her mentor Dr. Robert Feldman, and assisted with the diagnosis of neurotoxicant-induced neurological dysfunction; (e) she also completed courses in neuroimaging and neuropsychological assessment; (f) Dr. Ratner has published on these topics and has lectured in neurotoxicology and the diagnosis of neurotoxic effects in humans at both Boston University and Harvard's medical schools.

B. Christine Oliver

In general, the defendant contends that Dr. Oliver is not qualified to testify as an expert because she lacks experience and training in certain *specific* practice areas, such as neuro-toxicology, epidemiology, and the law, and yet more specifically, regarding ALS and toluene.

Dr. Oliver is not being offered as an expert in neurology or neurotoxicology, nor the law. She is being offered as an expert in "occupational medicine" (the same field as that of the defense expert Hashimoto). She is beyond question qualified by "knowledge, skill, experience, training, or education" as an expert in occupational medicine. Occupational medicine is a recognized specialty in medicine that deals with illness and/or disease caused by workplace (or environmental) exposure(s) to toxins, which is directly relevant to this case. Dr. Oliver has engaged in epidemiologic research and teaching, the clinical evaluation and treatment of patients, and administrative and policy work in the area of occupational disease for more than 20 years. She has served as a consultant to both state and federal governments in her capacity as a board certified physician and

scientific investigator in the area of occupational medicine. She is also board certified in internal medicine.

In addition to an MD degree, Dr. Oliver holds a Master of Public Health (MPH) degree and a Master of Science Degree in occupational health, both from the Harvard School of Public Health. Each involves course work in biostatistics and epidemiology – both applied by Dr. Oliver in her research in the area of occupational medicine. Neurology was not only part of her course curriculum and clinical rotations in medical school, but also a part of the practice of internal medicine which Dr. Oliver practiced during her post-graduate training and, thereafter, as a primary care practitioner.

Dr. Oliver has instructed medical students and others on the neurotoxic effects of solvents generally and toluene specifically. Defendant states that Dr. Oliver "is not an epidemiologist," (perhaps incorrectly believing that a certification process exists for epidemiology). Dr. Oliver, however, does consider herself to be an epidemiologist, having received training in that field. See Deposition of Christine Oliver ("Oliver Dep."), page 27, at **Tab 2**.

Defendant also asserts that, because Dr. Oliver "is not an attorney," she cannot offer opinions as to whether defendant breached industry standards. This is not a *Daubert* issue, and Dr. Oliver is not offered as a legal expert. While an expert generally cannot testify as to whether a defendant was negligent, experts commonly testify on industry practices. *Levin v. Dalva Bros.*, 459 F.3d 68, 69 (1st Cir. 2006).

Dr. Oliver's opinion is that "Southwest Recreational Industries, Inc., d/b/a Martin Surfacing, was negligent: (a) in its failure to warn Mr. Allen and other athletic staff of the potential toxicity of the chemicals used in the installation of the Versaturf '360'

polyurethane flooring system; and (b) in its failure to ensure that these personnel were either adequately protected or vacated from the Field House during the installation process". Her opinion is based upon her knowledge and experience in the field of occupational medicine. She has spent over 20 years working with patients exposed to chemicals at work and working with both labor and management to make sure that workers and *bystanders* are protected in cases such as this. She has taught -- on numerous occasions -- the hierarchy of protection from toxic workplaces: substitution; engineering controls; and personal protective equipment, with education of those who need to know as a *sine qua non.* Dr. Oliver has read and interpreted thousands of Material Safety Data Sheets for toxic chemicals. She serves as medical director for a chemical company in Massachusetts, and prevention of exposure to toxic agents is an important part of her responsibilities in this respect. Education and warning is an integral part of prevention and of the practice of occupational medicine. As such, she is uniquely qualified to provide an opinion as to industry practices and the applicable standard of care.

C. William Ewing

Defendant alleges that "William Ewing does not have sufficient knowledge, skills, experience, training or education related to the subject matter at hand, and therefore are (sic) not qualified to provide an expert opinion." After making this blanket allegation, defendant fails to point out any inadequacies in Mr. Ewing's training or education as an industrial hygienist that would render his opinion inadmissible. A review of Mr. Ewing's curriculum vitae reveals twenty-nine years spent conducting industrial hygiene and indoor air quality studies, including over 300 field investigations. His formal

education includes courses in toxicology and air quality assessments, along with a B.S. in biology. He is certified by the American Board of Industrial Hygiene as an Industrial Hygienist, and has published extensively. There are no shortcomings in his education or experience which would leave him unqualified to render an expert opinion in this matter.

Defendant dismisses Mr. Ewing's opinion as "speculative guesswork" without "any scientific foundation," and states that, applying the principles of *Polaino v. Bayer Corp.*, 122 F.Supp.2d 63 (D. Mass. 2000), should not be admitted as expert testimony. *Polaino* bears no similarity to the situation involved here. The expert in *Polaino* offered an opinion regarding an alleged design defect in a film processor, yet he had no experience or training in mechanical engineering. Although his opinion asserted that the plaintiff was injured by elevated levels of fumes released during operation of the machine in question, he never ascertained whether a*ny* fumes were released during its operation, much less whether elevated levels were encountered. These are the reasons the court rejected his opinion as resting on "unverified assumptions, speculation and guesswork." *Id.* at 69.

Mr. Ewing's opinion does not suffer from these shortcomings. First and foremost, his opinion does not stray into fields in which he has an inadequate background or education. Secondly, Mr. Ewing has detailed information regarding the types and amounts of solvents used, and the manner and timing of their application. He has investigated the ventilation system in use at the Holy Cross Field House, along with climatological data for the period in question. As a result, his opinion is not based upon speculation or unverified assumptions, but rather is the result of meticulous investigation, utilizing all available data, in a field in which he is highly qualified.

For all of the foregoing reasons, plaintiffs' experts are more than sufficiently qualified.[2]

III. ARGUMENT No. 2: GENERAL CAUSATION

In his attacks on plaintiff experts Ratner and Oliver in particular, defense counsel repeatedly asserts: If there are no known causes of ALS, and if there are no epidemiological studies which examine specifically toluene and ALS, one cannot opine that toluene or any other neurotoxic solvent can hasten the early onset of ALS.

There are several fatal flaws in this logic, both scientific and legal:

1. Defense counsel fails to support this assertion with any science. He offers nothing from his own expert, from the medical literature or elsewhere to support his bald statements;

2. As many times as he writes the phrases, it does not change the truth: this case is NOT about 'causation'; plaintiff is NOT claiming that toluene or any solvent causes ALS. This is a case about hastening the early onset of the ALS disease which lay dormant in Coach Allen and which, later in his life, would have manifested. As plaintiffs' experts explain in their report and will further explain at the evidentiary hearing in this matter, we need not know the causes of ALS, or whether solvents cause ALS, to prove to a reasonable degree of scientific certainty that a known neurotoxin like toluene (or other similar solvents) can alter the course of a known neurodegenerative disease like ALS, for example, by hastening the early onset of symptoms and the disease course. The focus here is, mainly, on the biological plausibility of how this is so,

[2] Again, of note, defendant has not offered any experts to "counter" plaintiff experts Ratner and Ewing; he offers only a lawyer/physician board certified in occupational medicine, Dr. Dean Hashimoto.

utilizing the generally accepted methods of toxicology and pharmacology so well known to Dr. Ratner. Indeed, no where in these attacks on Ratner, is there even one sentence which criticizes the toxicological/pharmacological methods of assessment used by plaintiffs' expert, nor can there be, as defendant has chosen not to disclose an expert with the same background as Dr. Ratner.

3. "Biological plausibility" is a determination, based on existing knowledge about human biology and disease pathology, that a given agent can cause a disease. *Reference Manual on Scientific Evidence* (2d ed.) at 388. Biological plausibility supports a general inference of causation. *Id.* That the criteria of biological plausibility is met is demonstrated by the following quote from a basic text on epidemiology: "Biological plausibility implies that a known biological mechanism is capable of explaining the relationship between the cause and effect. For instance, hypertension is a biologically plausible contributory cause of strokes . . . because the mechanism for damage is known and the type of damage is consistent with that mechanism."[3]

4. As plaintiffs' expert epidemiologist Richard Clapp (whom defense has chosen NOT to challenge and who will appear live at the evidentiary hearing to assist the Court) explains in his own report, not every case requires epidemiology, and not every notion is capable of being studied through the use of epidemiology. Dr. Clapp has reviewed the methods utilized by Dr. Ratner, and has applauded her thorough, scientific process; whereas Dr. Clapp

[3] Riegelman, R.K., Hirsch, R.P., *Studying a Study and Testing a Test: How to Read the Health Science Literature* 44 (3d ed. 1996).

strongly criticizes the defense expert Hashimoto, for failing to consider ALL the scientific evidence.

5. Defendant relies on a decision by Judge Saris, *Sutera v. Perrier Group of America Inc.*, 986 F. Supp. 655 (D. Mass. 1997), for the proposition that in toxic tort cases, epidemiology is necessary for plaintiff to meet his burden of proof. In *Sutera*, the plaintiff claimed that his consumption of trace levels of benzene in his Perrier water caused his leukemia. Plaintiff offered only the opinions of an oncologist who believes that, because benzene is a known carcinogen, any level can cause leukemia. No benzene was detected in sample Perrier bottles by experts commissioned by plaintiff's counsel. No governmental tests ever detected benzene in Perrier product. Plaintiff offered no studies which associate leukemia with trace levels of benzene. Judge Saris found the expert not qualified and his scientific evidence unreliable. But contrary to the defense position asserted here, nowhere in her decision did Judge Saris proclaim that epidemiology was required in all toxic tort cases.

6. Notwithstanding the foregoing, there is indeed epidemiology which generally supports the plaintiffs here, associating solvents with ALS (see *infra*); and just as important, there are no studies which contradict the position taken by plaintiffs' experts. But as plaintiffs' experts explain in their reports and will further explain at the evidentiary hearing, there are no studies which examine specifically toluene's (or any one solvent's) association with ALS for very good and practical reasons: it would take too long and cost too much, and no

entity – whether the chemical industry or the government or a private party – is motivated to pay for and conduct such a study.

7. Plaintiffs are not required to prove every proposition with a scientific study. *See Heller v. Shaw Indus., Inc*., 167 F.3d 146, 155 (3d Cir. 1999) ("we do not believe that a medical expert must always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness."). As the Supreme Court acknowledged in *Daubert*, "some propositions…are too particular, too new, or of too limited interest to be published." *Daubert*, 509 U.S. 579, 593.

8. Finally, before addressing expert-specific attacks, the Court is reminded that the burden here on plaintiffs is not, as defendant suggests in his various *Daubert* motions, to prove the "actual and proximate" cause by which Coach Allen's course of ALS was hastened; rather, as the case law makes clear, plaintiff need only show that Coach Allen's exposure to toluene and/or other neurotoxic solvents were a substantial contributing factor to hastening the early onset of his ALS. See *infra*.

A. Marcia Ratner

Dr. Ratner has presented a 33-page, single-spaced report to explain her methods and opinions as to both general and specific causation. Page limits do not permit us to repeat the full opinion here, but it is attached to, and summarized in **Plaintiffs' Affirmative Motion**. Her general causation opinion can, however, be boiled down to its essence quite easily: it is generally accepted in neurotoxicology (Dr. Ratner's area of expertise -- an area not shared by defendant's expert) that neurotoxicants have the

capability to alter the course of neurodegenerative disorders, including by hastening the onset of symptoms. Toluene is a known and accepted neurotoxin (defendant's expert agrees) and ALS is a known and accepted neurodegenerative disease (again, defendant's expert agrees).

Defense counsel argues, Ratner's "theory" is impossible to prove because we do not know the cause(s) of ALS and no studies exist to prove specifically that toluene causes/hastens ALS. Ratner's opinion, however, is not a theory, but rather a generally accepted proposition in neurotoxicology; and it matters not that no specific studies exist on toluene and ALS. As Dr. Ratner explains at length in writing and will further explain live in court, it is generally accepted that neurotoxicants damage neurons and neurodegenerative disease damages neurons, so here we are looking at an additive effect of two independent causes of neuronal damage that can interact to hasten the course of the disease if they occur in the same individual. One does not need to know or prove anything other than that the patient suffered a neurodegenerative disease and that he was sufficiently exposed to a neurotoxicant to know that, necessarily, the latter will affect the former. Dr. Ratner explains the "how" (i.e. the biological plausibility by which the neurotoxicant toluene interacts with the effects of the neurodegenerative disease ALS) in substantial detail in her report. Whether the effect is a 'substantial contributing factor', as plaintiffs assert here, is addressed in plaintiff's experts' "specific causation" opinions which are addressed below.

B. Christine Oliver

Defendant discounts Dr. Oliver's opinion as "nothing more than a speculative hypothesis," which cannot pass the *Daubert* test. Defense counsel cites liberally to *Allen v. Pa. Eng'g Corp.*, 102 F.3d 194 (5th Cir. 1996) which, he claims, is "directly on point." It is not. *Allen* is quite different in a number of important ways. *Allen* involved exposure to ethylene oxide (EtO), a substance which had been widely studied, particularly in terms of occupational exposure; however, none of the studies found a correlation between EtO and brain cancer. Indeed, not only were there no studies supporting plaintiff's position in *Allen*, there were numerous studies involving thousands of workers that found just the *opposite*, that there was *no* correlation between EtO and brain cancer.

No such studies exist here contradicting plaintiffs' experts' opinion. Defendant repeatedly misrepresents Dr. Oliver's opinion, by referencing only toluene, when in fact her opinion clearly addresses *all* the solvents to which Coach Allen was exposed. The analogy to *Allen* then becomes even less appropriate, as **epidemiological studies do exist which find a correlation between solvent exposure and ALS, and other neuromuscular diseases**.

Finally, in *Allen* the plaintiff's 'exposure' evidence bordered on the non-existent, or "mere guesswork" as there was no direct evidence; so, exposure evidence was gleaned only through extrapolation from data based on other hospitals during the 1970s. But here, Coach Allen's exposure is documented through first-hand accounts contained in co-worker affidavits, in addition to the Coach's own accounts of exposure. The *Allen* plaintiff also suffered additional EtO exposure from smoking, a fact discounted by his

experts but of obvious concern to the *Allen* court. There is no evidence here that Mr. Allen was exposed to the neurotoxic solvents at issue except as caused by the defendant.

In reaching her opinions here, Dr. Oliver considered detailed medical records of Coach Allen's clinical course around the time of and subsequent to his exposure to solvents, including toluene, in the Field House of The Holy Cross College in May/June 2001. Included in these records is family history, past medical history and habits such as cigarette smoking and alcohol use, and review of systems. He had no family history of ALS and no other putative risk factors for ALS (with the *possible* exception of thyroid disease, which is discussed further below).

Importantly, in reaching her opinions Dr. Oliver also considered *all other available information relevant to the case*. This information includes publications in the medical and scientific literature. At least five peer-reviewed studies have shown a twofold or greater increase in risk for ALS associated with solvent/chemical exposures (or in one study "fumes and dust") (Gunnarsson et al, 1992;Chancellor et al, 1993; McGuire et al, 1997; Mitchell et al, 1995; Morahan and Pamphlett, 2006). McGuire et al (1997) examined associations between ALS and exposure to "benzene, toluene, or xylene"; using an exposure assessment by a panel of four experienced industrial hygienists, the investigators observed a 70% increase in odds of exposure to these solvents in subjects with ALS (OR 1.7 (95% CI=0.9-3.0)).

With regard to the question of early onset of disease and more rapid progression in Coach Allen's case, Dr. Oliver reviewed three epidemiologic follow-up studies published in peer-reviewed journals (Mitchell, 1995; Chio, 2002; Millul, 2005). Mean age at onset was 61, 62.8, and 63 (spinal-onset) years, respectively. Each showed that

age at onset was inversely related to survival – with shorter survival times for those who were younger at disease onset. In the study by Millul et al (2005), mean survival from onset of symptoms in those ages less than 55 years, was 52.1 mos. Coach Allen was 45 years of age at onset of his ALS symptoms and his survival time was 32 months. The study by Gunarrsen et al (1992) showed odds ratios (OR) for exposure to any solvent among subjects with ALS to be 3.2 for cases ages 45-59 years, 1.1 for cases ages 60-60 years, and 0.9 for cases 70-79 years; OR was 25.1 (95% CI=3.6-175.8) for males with any solvent exposure and a "heritability".

In addition, Dr. Oliver reviewed, and concurs with, the expert reports of Dr. Ratner and Mr. Ewing, addressing biochemical mechanisms and exposure variables, respectively.

All of this information taken together satisfies at least six of Sir Austin Bradford Hill's nine criteria for causation: consistency, temporality, biologic plausibility, coherence, experimental evidence, and analogy.[4] Thus, the methodology used by Dr. Oliver in arriving at her opinion that "…the time of onset and rate of progression of ALS in Mr. Allen's case were causally related to his exposure to solvent vapors and aerosols during the course of the installation of the Versaturf '360' flooring system in the Field House of The College of the Holy Cross" is both scientifically valid and relevant.

[4] To better aid scientists in their quest to infer causation, Sir Austin Bradford Hill suggested various factors one could consider to infer causation from association. The Hill guidelines were proposed in 1965 as a *suggested tool* for scientists to *consider* when faced with a question regarding causation. They do not require each to be established in order to distinguish causal from non-causal associations. Hill in fact concluded, "What I do not believe – and this has been suggested – is that we can usefully lay down some hard-and-fast rules of evidence that must be obeyed before we accept cause and effect. None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental question – is there any other way of explaining the set of facts before us, is there any other answer equally, or more likely than cause and effect?" Sir Austin Bradford Hill, *The Environment and Disease: Association or Causation?*, Proceedings of the Royal Society of Medicine, Section of Occupational Medicine 300 (1965)

IV. ARGUMENT No. 3: SPECIFIC CAUSATION

Defendant's three main assertions here are that:

1. Plaintiffs' experts Ratner and Oliver cannot reliably testify that toluene and/or other solvents were a substantial contributing factor to hastening the early onset of Coach Allen's ALS, if they cannot demonstrate Coach Allen's precise levels of exposure;

2. Plaintiffs' experts cannot rule out other possible contributing factors; and

3. 'Temporal proximity' -- the time between Coach Allen's exposure and the onset of symptoms of his ALS -- has no scientific value.

We address generally each point, followed by additional expert-specific points.

1. Plaintiffs Need Not Prove The Exact Level of Exposure.

As to the first point, the defendant confuses the real issue here: as explained in the **Plaintiff's Affirmative Motion** and also addressed below, this is not a case where it is necessary to prove a specific level of exposure; the un-rebutted evidence is that everyone exposed to the solvents at issue suffered neurologically adverse effects, which tells us without doubt that the exposure was at levels higher than permissible according to OSHA standards, and necessarily high enough to cause an "eggshell" like Coach Allen to suffer the hastening of the early onset of his ALS.

OSHA takes the position that persons at risk for neurological disease should not be exposed to toluene, because toluene is a neurotoxicant. A person with neurological disease is more brittle than a healthy person and therefore more vulnerable to the toxic effects of the toluene and other neurotoxicants. As a result, levels of exposure that would not harm a healthy individual can cause damage to a sick individual, as was the case here.

Defendant argues that plaintiffs are unable to provide an opinion as to "the length, the extent, or the amount of toluene" that Coach Allen was exposed to by defendant.

While plaintiffs cannot establish the *precise* duration or concentration of exposure, there is sufficient evidence of both to allow experts Ratner and Oliver to reach their opinion.

The installation process was started on May 21 and completed on June 6, according to defendant's records. The diary kept by Coach Allen and sworn testimony of his co-workers (all attached to the **Plaintiffs' Affirmative Motion**) indicate that he remained at work during this period of time and remained after he let his co-workers go home *because of health problems caused by exposure to the toxic fumes*. He was attempting to get things in order for the upcoming football camp. Thus, duration is known in general terms.

The symptoms documented by Coach Allen and his co-workers are classic symptoms of central nervous system neurotoxicity: headache, dizziness, nausea, disorientation, and an indicator of level of exposure. Burning of eyes and throat experienced by one colleague is evidence of irritant effects of solvents. The OSHA PEL for toluene is 200 ppm and the PEL recommended by the National Institute for Occupational Safety and Health (NIOSH) is 100 ppm. Hathaway and Proctor (Chemical Hazards of the Workplace, 2004) state that "Controlled exposure of human subjects to 200 ppm for 8 hours produced mild fatigue, weakness, confusion, lacrimation, and paresthesias of the skin. At 600 ppm for 8 hours, other effects included euphoria, headache, dizziness, dilated pupils, and nausea." The similarity of these effects to those experienced by Coach Allen and co-workers permit reasonable inferences to support plaintiffs' experts' that the levels of exposure were *in excess of the OSHA PEL.*

Further, Mr. Ewing's expert report provides informed estimates of the quantities of solvents used and evaporated during the floor installation process. Of the chemical

products used in the process, three were spray-applied: Martin 2164 Urethane Primer, Martin AP Concentrate, and Martin S2951 Tan Flat urethane coating. The solvents contained in these products are volatile and evaporated once applied. The spray application results in aerosolization of the liquid solvent as it is applied, increasing its availability for inhalation. Thus there were two mechanisms by which the solvents were airborne and two time periods during which this occurred. Coach Allen and his colleagues on the second floor of the Field House were working in a relatively enclosed space with windows closed. That the spray applicators were not affected is understandable given that they were using respiratory protection (Crecelius Aff. ¶ 6(d), attached to the **Plaintiff's Affirmative Motion**), a benefit not afforded to Coach Allen and other bystanders in the Field House.

Defendant disparages Ratner and Oliver's opinions as being based upon "anecdotal" evidence of "witness description of odors." The affidavits provided by Coach Allen's co-workers, and his own documentation of his exposure and symptoms, go far beyond "witness description of odors." They document the fact that Coach Allen and his co-workers all suffered various neurological problems, and that those problems occurred at the same time they were exposed to noxious fumes produced during the defendant's resurfacing of the gym floor. It is unclear exactly what defendant means by use of the term "anecdotal," but as Dr. Oliver explained at her deposition, the affidavits provide the same kind of reliable information as that accepted in peer-review published case studies. Oliver Dep., pages 42-43 (**Tab 2**).

The fact that Coach Allen was predisposed to the eventual onset of a neurodegenerative disease (ALS) that made him more susceptible to the toxic effects of

Toluene and/or other solvents, does not relieve defendant of liability. He is the classic eggshell plaintiff, and defendant must take him as they found him. *Figueroa-Torres v. Toledo-Davila*, 232 F.3d 270, 275 (1st Cir. 2000); *see also* Restatement 2d of Torts, § 461. The Court in *Higgins v. Delta Elevator Service Corp.* stated:

> [w]here an injury arising from a cause which entails liability on the defendant combines with a pre-existing or subsequently acquired disease to bring about greater harm to the plaintiff than would have resulted from the injury alone, the defendant may be liable for all the consequences. If the injury causes or contributes to cause the development of a preexisting disease, the person liable for the injury is liable also for the resulting aggravation. The wrongdoer must be held responsible for the harmful results of the combined effects of his wrongful act and the disease.

Higgins v. Delta Elevator Service Corp., 45 Mass.App. 643, 649, n.8 (1998).

Many courts, including in Massachusetts, have held that minimum dose evidence is not a requirement to establish causation. See, e.g.,*Payton v. Abbott Labs*, 780 F.2d 147, 157 (1st Cir. 1985); *Ruiz-Troche v. Pepsi Cola*, 161 F.3d 77 (1st Cir. 1988); see also *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 264-266 (4th Cir. 1999) (holding an expert's causation testimony, which was based on differential diagnosis, to sufficiently reliable to be admitted, despite the lack of "threshold level" evidence).

In *Westberry*, the plaintiff brought a products liability action against his employer, claiming that a talc product used in the employer's manufacturing process caused his severe sinus problems. Among the employer's challenges to plaintiff's proffered expert testimony was that plaintiff's expert could not "rule in" talc as the cause of plaintiff's injury because he had no means of accurately assessing the threshold level of exposure required to produce the onset of plaintiff's symptoms. *Id.* at 263. The Fourth Circuit rejected all of the employer's assertions. It held:

> While precise information concerning the exposure necessary to cause specific harm to humans and exact details pertaining to the plaintiff's exposure are beneficial, such evidence is not always available, or necessary to demonstrate that a substance is toxic to humans given substantial exposure and need not invariably provide the basis for an expert's opinion on causation.

Id. at 264 (citation omitted) (noting that "even absent hard evidence of the level of exposure to the chemical in question, a medical expert could offer an opinion that the chemical in question caused plaintiff's illness").

The Third Circuit Court of Appeals in *Kannankeril v. Terminix Intern., Inc.*, 128 F.3d 802 (3d Cir. 1997) rejected the defendant's argument that the plaintiff's expert was unreliable because he failed to consider a threshold level of exposure necessary to produce plaintiff's injury. Instead, the court concluded that plaintiff's expert's testimony was reliable because he based his causation opinion on a differential diagnosis: "[H]e considered the facts of the plaintiff's exposure, the temporal relationship between exposure and disease, the scientific literature establishing an association between [exposure and symptoms], the plaintiff's medical records and history of disease, and exposure to or the presence of other disease causing factors." *Id*, at 809. "All of these factors, according to the FJC's [Federal Judicial Center] Reference Manual, are appropriate criteria in forming an opinion on causation." *Louderback v. Orkin Exterminating Co., Inc.*, 26 F. Supp. 2d 1298, 1306 (D. Kan., 1998) (discussing and following the opinion of *Kannankeril*); see also *Bednar v. Bassett Furniture Mfg. Co., Inc.*, 147 F.3d 737 (8th Cir. 1998).

Defendant supports his contrary proposition by relying on the *Allen* case, examined in detail above. Again, in *Allen*, the estate of a hospital worker sued the manufacturer of ethylene oxide, to which the worker had been exposed, alleging the

exposure caused his brain cancer. The *Allen* court found that no level of exposure was presented by the evidence. That is not the case here, where only the precise level of exposure is incapable of determination.

2. Plaintiffs Need Not Rule Out All Other Potential Contributing Factors.

As to the second point, plaintiffs' experts are not required under the controlling law to 'rule out' all other causes, but only to show that toluene and/or the other solvents were a substantial contributing factor in hastening the early onset of Coach Allen's ALS.

Differential diagnosis is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated. *Baker v. Dalkon Shield Claimants Trust,* 156 F.3d 248, 252-53 (1st Cir. 1998). Proper differential diagnosis does not require that all possible causes be ruled out, only that the most probable one be identified.

In Massachusetts, differential diagnosis is an accepted methodology used in determining the cause of an illness. *Hammond v. Bedford Great Road CVS, Inc. et al*, 9 Mass. L. Rep. 104 (1998). Contrary to defendant's contentions, an expert need not conclusively rule out all possible causes in performing a differential diagnosis. As Superior Court Judge Neel explained in *Hammond*:

> Courts have insisted time and time again that an expert may not give opinion testimony to a jury regarding specific causation if the expert has not engaged in the process of differential diagnosis. Indeed, in the *Daubert* case itself the Supreme Court demanded that the expert 'explain how…he was able to eliminate all other potential causes of [the] birth defects.' **This does not mean that a medical causation expert must eliminate all possible causes of an alleged condition,** nor does it mean that the expert must always make a physical examination of the plaintiff or conduct a battery of tests aimed at eliminating competing causes of the plaintiff's condition. **Nevertheless it is true that 'at the core of differential diagnosis is a requirement that experts at least consider alternative causes**—this almost has to be true of any technique that tries to find a cause of something.' *Hammond,* 9 Mass. L. Rep., *22-23. *citations omitted.*

(Emphasis added).

The process of differential diagnosis requires that the physician weigh all the plausible explanations for the patient's symptoms and come to his or her best medically supported conclusion as to the cause, however, the physician "need not exclude every possible cause of the plaintiff's symptoms, but must be distinguished from mere guesses as to the probable cause." *Rhilinger v. Jancsics, et al.,* 8 Mass. L. Rep. 373, * 40 (1997) (*quoting Blanchard's Case*, 227 Mass. 413, 415 (1931) (denying motion to exclude plaintiff's experts and holding that expert opinions should show that the exposure to chemicals was the "reasonably probable cause" of her condition); *See also In re Paoli Railroad Yard PCB Litig.*, 35 F.3d 717, 759 n.27 (3rd Cir. 1994), *cert. denied*, 513 U.S. 1190 (1995) ("the standard techniques of differential diagnosis are reliable"); *Kannankeril v. Terminix Intern., Inc.*, 128 F.3d 802, 807 (3rd Cir. 1997) ("We have recognized 'differential diagnosis' as a technique that involves assessing causation with respect to a particular individual).

Any other standard would be inconsistent with the rule of law, that plaintiffs' burden is to prove causation by a preponderance of the evidence, i.e., more likely than not. It also would conflict with the "substantial contributing factor" standard. Plaintiffs' burden is not to prove the sole cause of Coach Allen's early onset of ALS – proving that toluene and/or other solvents were a substantial contributing factor is sufficient. *Johnson v. Summers*, 411 Mass. 82, 88 (1991); *accord, O'Brien v. Kobrin*, 11 Mass. L. Rep. 593, *23-5 (2000); *Frotten v. Masskey Dev. Corp.*, 2001 Mass. Super. LEXIS 573, *5-8 (2001) (jury should decide whether negligent conduct was a substantial factor in causing the plaintiff's injury); *See also* Restatement (Second) of Torts § 432.

3. The Value Of Temporal Proximity Is Well-Accepted In Law and Science.

Defense counsel's notion, that "[e]xpert testimony should not be based upon temporal proximity ……", flies in the face of one of the tenets of occupational medicine and of Sir Austin Bradford Hill, and the *Reference Manual on Scientific Evidence*. Temporal associations are *one* of the ways in which causal associations are established to a reasonable degree of medical certainty.

A number of courts have looked favorably on medical testimony that relies heavily on a temporal relationship between an illness and a causal event, particularly where the temporal relationship is strong and a thorough differential diagnosis is performed.

Contrary to the defense position, Massachusetts courts have held that "close temporal proximity between two events may give rise to an inference of causation." *See Nethersole v. Bulger*, 287 F.3d 15, 20 (1st Cir. 2002) ("close temporal proximity between two events may give rise to an inference of causal connection."); *see also Continental Insurance Co. v. Arkwright Mutual Insurance Co.*, 102 F.3d 30, 36 (1st Cir. 1996) (". . . there may be other reasons why the short circuit may have occurred, but it's clear that the short time frame between the flood and the short circuit allows the court to reasonably infer that the damage was caused by flooding.").

Temporal proximity can provide a reasonable and sometimes even compelling basis for assessing causation where, as here, there is other supporting evidence. *See also Reference Manual on Scientific Evidence*, 2nd Ed. 2000, p. 426, n. 63; *National Bank of Commerce v. Dow Chem. Co.*, 965 F. Supp. 1490, 1525 (E.D. Ark 1996 ("[T]here may be

instances where the temporal connection between exposure to a given chemical and subsequent injury is so compelling as to dispense with the need for reliance on standard methods of toxicology."). *Accord, Kannankeril v. Terminix Intern., Inc.,* 128 F. 3d 802, 809 (3d Cir. 1997) (the court noted the doctor's opinion "the temporal relationship and the nature of her complaints lead me to conclude that with reasonable medical certainty, the cause of [the plaintiff's] Central Nervous System manifestations of toxicity is exposure to Dursban in 1989 to 1990"); *Louderback v. Orkin Exterminating Co., Inc.*, 26 F. Supp. 2d 1298, 1306 (D. Kan., 1998) (discussing and following the opinion of *Kannankeril*).

A. Marcia Ratner

In this case, Dr. Ratner applied and followed with integrity the very algorithm for assessing specific causation in neurotoxicity tort cases, which she co-authored with the late Dr. Robert Feldman, and which has been published and subjected to peer-review. Her conclusions are based primarily on her general causation assessment; the presence of neurotoxicants including but not limited to toluene having been present in the work place at levels high enough to cause overt neurological symptoms; the chronological relationship between disease onset and exposure; and her differential diagnosis. Dr. Ratner considered all possible causes per her algorithm and could not find a more plausible or probable explanation.

Contrary to the defense assertion, Dr. Ratner did not arbitrarily assign the greatest value to Coach Allen's exposure, given: (a) the lack of a family history of ALS; (b) the known direct neurotoxic effects of toluene (and other solvents) and their ability to interfere with the body's ability to defend itself against oxidative stress; and (c) the

chronologic and exquisitely temporal relationship between the exposure event and the onset of the symptoms of ALS.

B. Christine Oliver

Although defendant asserts that Dr. Oliver's differential diagnosis is "without foundation," she based it upon an examination of Mr. Allen's detailed medical records and his family history, and ruled out as other possible causes: trauma, physical activity, cigarette smoking, infection, welding, and heavy metals. Only thyroid disease emerged as another possible contributing factor. But again, the plaintiffs do not have the burden of eliminating all other possible causes; only that the chemical(s) in question were, more likely than not, a substantial contributing factor.

Defendant suggests that Dr. Oliver's opinion "is nothing more than an opinion that Mr. Allen suffered from Multiple Chemical Sensitivity." Defendant's suggestion displays a complete lack of understanding of plaintiff's position. Dr. Oliver has *never* offered the opinion that Mr. Allen suffered from multiple chemical sensitivity (MCS). When defendant specifically asked at her deposition if in her opinion he suffered from MCS, she answered "no". Oliver Dep. at 14, **Tab 2**.

What Dr. Oliver has repeatedly stated is that Mr. Allen was exposed to a *number* of solvents, including toluene, that are known toxicants of the central nervous system, and that this exposure hastened the onset of his ALS. Her opinion regarding onset and progression of Mr. Allen's ALS is based upon evidence provided in the scientific literature and described above regarding usual age at onset, increased OR for any solvent exposure in younger vs. older age groupings of subjects with ALS, and Dr. Ratner's

expert report regarding specific biochemical pathways in the development of ALS, as well as the exposure information also described above.

C. William Ewing

Defense counsel argues that Mr. Ewing's opinion should be excluded because plaintiffs are unable to provide an opinion as to "the length, the extent, or the amount of toluene" that Coach Allen was exposed to by defendant. It must be noted that Mr. Ewing does not restrict his opinion to toluene exposure, but addresses all the solvents used in the refinishing process. As explained previously, while plaintiffs cannot establish the *precise* duration or concentration of this exposure (through no fault of the plaintiffs), there is sufficient evidence of both to allow Mr. Ewing to reach his opinion. The installation process was started on May 21 and completed on June 6, according to defendant's records. The diary kept by Mr. Allen and testimony of his co-workers indicate that he remained at work during this period of time and remained after he let his co-workers go home *because of health problems caused by exposure to the toxic fumes*. In investigating Mr. Allen's exposure, Mr. Ewing also examines the timing and duration application process. Thus, duration is known in general terms.

Defendant's assertion that Mr. Ewing, by his own admission, is without "any knowledge" regarding the duration or concentration of Mr. Allen's exposure to toluene, is both patently false and misleading. As previously noted, Mr. Ewing does not focus his investigation on toluene alone, but *all* of the solvents to which Mr. Allen was exposed. To characterize the substantial information utilized by Mr. Ewing as being so inconsequential as to render him "without knowledge" regarding the duration and concentration of exposure goes beyond hyperbole, it is intellectually dishonest.

V. CONCLUSION

For all of the foregoing reasons, this Court should deny defendant's motions to exclude plaintiffs' causation experts and should rule that each challenged expert -- Ratner, Oliver and Ewing -- may testify at trial, as requested in plaintiffs' own affirmative motion.

Respectfully Submitted,
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Dated: December 3, 2007

Certificate of Service

I hereby certify that a copy of the foregoing was served this day via ECF to the following counsel:

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Monozygotic Twins Discordant for Huntington Disease After 7 Years

Joseph H. Friedman, MD; Martha E. Trieschmann, MD; Richard H. Myers, PhD; Hubert H. Fernandez, MD

Arch Neurol. 2005;62:995-997.

ABSTRACT

Background Huntington disease (HD) has only rarely been identified in identical twins. All described twins have had disease onset within 1 year of each other, suggesting that disease onset is determined solely by genetic influences.

Objective To describe a unique set of monozygotic twins in whom clinical HD onset is at least 7 years apart.

Design A 71-year-old woman was diagnosed as having HD based on medical history, physical examination results consistent with HD, and a CAG trinucleotide repeat number of 39 in the *HD* gene on chromosome 4. Her onset was 6 years earlier. Her genetically confirmed identical twin, carrying the same number of CAG repeats, was neurologically healthy when examined the next year. Only the HD-manifest twin had chronic bronchitis, rheumatoid arthritis, type 2 diabetes mellitus, and chronic anemia. Both had hypertension.

Conclusions To our knowledge, this is the first report of monozygotic twins discordant for HD by more than 2 years. The onset of HD symptoms in a patient with 39 triplet repeats at least 7 years earlier than her identical twin suggests the possibility that the disease may be initiated (or delayed) by environmental factors. We have identified increased cigarette use and longer exposure to various industrial toxins as potential explanations for the earlier onset in one twin.

INTRODUCTION

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Huntington disease (HD) is an autosomal dominant disorder characterized by the triad of chorea, dementia, and behavioral abnormalities. The abnormal gene is characterized by an excess number of CAG trinucleotide repeats that code for glutamine in the Huntington protein. People with 40 or more repeats are thought to always develop the disease if they live long enough. Repeats in the 36 to 39 range are in a gray zone in which penetrance is less than 100%. Factors that determine whether the disease appears in patients with an indeterminate number of repeats are unknown. In

general, the more repeats, the earlier the disease onset, but violations of this rule are common.

REPORT OF A CASE

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A 71-year-old woman was brought for evaluation of a progressive decline in gait and cognition. The problem began about 6 years earlier, around the time of a surgical repair of an abdominal aortic aneurysm. She had chronic obstructive pulmonary disease due to cigarette smoking, type 2 diabetes mellitus, rheumatoid arthritis, and chronic anemia, ascribed to the rheumatoid arthritis and hypertension. She had lost 9 kg in recent months and was thought to have depression. A feeding tube had been placed. Her brain magnetic resonance image, unchanged from a study 1 year prior, showed mild atrophy, small-vessel ischemic disease, and several punctate areas of mineralization in the cortex. No caudate atrophy was present. Her medications were prednisone, alendronate sodium, sertraline hydrochloride, amitriptyline hydrochloride, insulin, atenolol, omeprazole sodium, epoetin alfa, iron sulfate, and multivitamins. She had stopped smoking about 6 years earlier. She was fully oriented, but thought Richard Nixon was the president. Although she registered 3 objects, she could recall 0 at 2 minutes. Her clock drawing was markedly abnormal. She could spell the word "farm" but spelled it backward as "marf." Her cranial nerve findings were normal, including eye movements. She had brisk reflexes, normal strength, generalized chorea, and a moderate degree of ataxia in her arms and legs. She was unable to stand without being pulled up. Her base was wide. Her stride was reduced, and her balance was poor. Gene testing revealed an *HD* gene with 39 CAG repeats in one allele and 12 in the other.

The patient informed us that she had an identical twin. The identical twin was examined by the same group of 3 movement disorders specialists (J.H.F., M.E.T., and H.H.F.) who had seen the affected twin, about 9 months later, and the identical twin was healthy. Eighteen months after the initial contact, she reported over the telephone that she was still healthy. She was also genetically tested, and found monozygotic (MZ) with the same CAG repeat numbers in the *HD* gene. The asymptomatic twin had hypertension but none of the other disorders of her sister. She had stopped smoking cigarettes at the age of 35, whereas the twin with manifest HD had stopped at the age of 65, after her chronic obstructive pulmonary disease had developed. There were no differences in childhood illnesses, alcohol use, prescribed drug use as children, or caffeine intake. The birth home was across the street from a factory that produced large machines used to manufacture precision cutting tools from the late 1800s to 1987. "Numerous chemical spills and leaks occurred over the years."[1] The air was described as polluted, and in 1993, 2 years after the factory closed for the second time, the site was designated a federal toxic site requiring cleanup. It was considered primarily a "brownfield" site, containing mainly oil products, and the principal chemicals of concern identified were dichloroethene, trichloroethylene, and vinyl chloride. Both twins had been equally exposed to the factory's toxins until the age of 23, when the asymptomatic twin moved away. The twin with manifest HD remained in her original house. The asymptomatic twin moved about 3.2 km away, within the same neighborhood, in New Bedford, Mass. Although the factory closed first in 1985, it was reopened from 1988 to 1991, and samples of air and soil are still analyzed by health department authorities, with reports provided to neighbors. The asymptomatic twin lives sufficiently far away that the air and soil in her neighborhood are not tested. A dietary/nutritional, lifestyle, and medication intake interview was performed, showing no significant differences.

The twins had 5 siblings, of whom 2 were still alive. None were known to have neurological or psychiatric problems, but have not been examined. None of the children of the twins are thought to be affected.

Tests to identify subclinical disease in the unaffected twin, such as positron emission tomography, were not attempted, because publication of the result would potentially identify the twin's disease status against her wish.

COMMENT

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Unlike Parkinson disease, in which environmental factors have been associated with disease risk, HD has been known as a genetic disorder with little, if any, environmental influence. At least 12 presumed or confirmed MZ twins with HD have been described,[2-6] and the data are mixed. Sudarsky et al[2] described MZ twins who had a similar age of symptom onset and motor and behavioral abnormalities despite having been raised in separate households from birth. In contrast, Georgiou et al[4] described a pair of twins who, although sharing identical CAG repeat lengths, had marked differences in clinical and behavioral symptoms. Oepen[5] and Bird and Omenn[6] described MZ HD twins who presented with variable movement disorders but a similar degree of cognitive dysfunction. Nevertheless, the age of symptom onset in these previously described twins had not been more than a couple of years apart.

Only on rare occasions have other dominantly inherited nervous system disorders shown discordance for disease onset.[7] A pair of MZ twins with familial amyloid neuropathy developed the illness 13 years apart.[8] In another report[7] of MZ twins, one had cerebral adrenoleukodystrophy by clinical examination and magnetic resonance imaging starting at the age of 10 years, whereas the other remained healthy 1 year later. Both had the same genetic mutation.

The occurrence of discordance for HD 7 years after onset in one twin suggests the possibility that environmental agents may have an influence on disease initiation. We were able to identify significant differences in exposures to cigarettes and to various industrial toxins, both of which were greater in the twin with manifest HD. We found no reports linking cigarette smoking and HD. At least one study[9] in a rodent model of HD suggests the possibility that environmental factors may retard the progression of the disease.

Although strokes can mimic or aggravate HD, it was unlikely that the symptomatic twin's small-vessel ischemic disease was contributory. This was an incidental finding, was minimal, and did not involve the basal ganglia or thalamus. Similarly, although there have been reports of increased incidence of diabetes mellitus in HD patients[10-11] and HD animal models,[12] there has been no suggestion that diabetes mellitus is a major contributor to the HD phenotype.[10-12]

Concordance rates in MZ twins for diabetes mellitus[13] are 57% at 10 years and 76% at 15 years. In one study[14] of concordance in patients with rheumatoid arthritis, there was a zero concordance rate in MZ twins in a point prevalence study, implying a lack of significant genetic correlation. The differences between the twins in these medical aspects are, therefore, not surprising, and may or may not be linked to their different susceptibilities to the *HD* gene abnormality.

Dietary influences on age of symptom onset in those with HD have been reported,[15] with higher milk intake associated with an earlier age of onset in a study of 51 families of patients affected with HD. Another study[16] showed high vitamin A and low vitamin C and niacin intakes in HD patients compared with control subjects. We found no differences in milk or vitamin consumption. However, the symptomatic twin used 7 prescription drugs and 3 over-the-counter medications that her asymptomatic twin never took.

Other potential factors that could have influenced the disparity in expression of the HD mutation in this pair of twins include the late age of onset and the borderline number of CAG repeats (39 repeats). It is possible that sensitivity to environmental factors might play a greater influence in marginal HD cases such as this one.

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UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS
C.A. NO. 05-40048-FDS

LAURA ALLEN, INDIVIDUALLY; And As ADMINISTRATRIX OF THE ESTATE OF DANIEL ALLEN; And As NEXT FRIEND OF TAYLOR ALLEN AND DANIELLE ALLEN; And MARK ALLEN,
Plaintiffs,

vs.

MARTIN SURFACING, A Division of SOUTHWEST RECREATIONAL INDUSTRIES; SOUTHWEST RECREATIONAL INDUSTRIES, INC., d/b/a MARTIN SURFACING,
Defendants.

DEPOSITION OF L. CHRISTINE OLIVER, M.D., taken on behalf of the Defendant, before June N. Poirier, Shorthand Reporter and Notary Public within and for the Commonwealth of Massachusetts, at the law office of Brent, Coon & Associates, 277 Dartmouth Street, Boston, Massachusetts, on Friday, November 2, 2007, commencing at 11:40 a.m.

DUNN & GOUDREAU COURT REPORTING SERVICE, INC.
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Q I know you never had an opportunity to treat Mr. Allen, but based on your review of the medical records, in your opinion did he suffer from any multiple chemical sensitivity?

A As far as I could tell from the record, no.

Q Have you ever published any paper relating to ALS or Lou Gehrig's disease?

A No.

Q Have you ever published any paper relating to the toxicity of toluene?

A No.

Q I'm going to show you Exhibit 3 and see if you recognize that.

A Yes. This is a list of trial and deposition testimony that I have given over the last five years.

Q I'd like to go through these for the next several moments. The first case, Gilberti versus Touro, that occurred in 2003, deposition in Boston in October '01, and then trial in New Orleans in 2003; is that right?

A Yes.

Q What was your involvement in that case?

Q And the clinical practice that you currently have, how often do you see patients --

A Well, let me take a step back. I think epidemiologists do not get board certified. I don't think there is a board certification process for epidemiology, at least as far as I know.

Q Do you hold yourself out as a epidemiologist?

A Yes. To the extent that I, during my medical school training and also my residency in occupational and environmental medicine, epidemiology was one of the subject matters that was included in the educational curriculum.

Q So are you saying that the education that you had with regard to epidemiology was provided to you in medical school and postgraduate?

A Yes.

Q Okay. Are you familiar with the opinion of Dr. -- Professor Richard Clapp in this case?

A I have not seen that.

Q Do you know Mr. Clapp?

A I do. Dr. Clapp.

Q Dr. Clapp has several initials after his name. Capital D.Sc, is that doctor of science?

described at lower levels of exposure to toluene not just toxic levels"?

A Read that again.

(Whereupon the question was read back.)

A I think it's possible. I think it would be very unusual. And in this case there were four individuals who experienced similar symptoms during the course of this exposure. I do not think it would be reasonable, nor do I believe that all four of these individuals were experiencing symptoms at lower levels of exposure because it's unusual, it's very unusual. It's possible. It could happen. It's unlikely to happen and it certainly is unlikely to happen in the case of four different people.

Q Let's talk about those four different people. Their reports of their symptoms is anecdotal, would agree or disagree with that?

A I don't think their report is anecdotal at all. I would disagree with that.

Q Could you use simply their reports in an investigative study of the effects of toluene without any independent testing such as urinalysis, expelled air, and blood work to verify the levels of toluene exposure?

A You could use it as a series of case reports. Case reports of four. There was a case report published in Clinical Toxicology in 1991, I believe, and there was an individual 38-year-old laborer who was spray painting trucks and heavy equipment in an enclosed space, and he developed -- and his total exposure was over a period -- was 24 hours spread out over a period of four days, so that was approximately six hours a day, and he experienced irreversible neurologic damage. In that case it was published in a peer-review journal. And the conclusion was that his exposure to the solvents that were used in this spray painting, and I believe the solvents were toluene and methylthio ketone. I can check that. I believe those were the two solvents. And nobody went in and measured the levels of exposure when he was doing this spray painting. That was one example of a case report that was published without specific levels of exposure.

Q When you say "the four individuals," are you including Mr. Allen in the four reports of symptomatology?

A I'm including Mr. Napolitano, Mr. Bradley